Bangkok 2004: Progress In Spite of Protest?

Veronica Miller, PhD
Director, Forum for Collaborative HIV Research
Washington, District of Colombia

EDITED BY TIM HORN

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When PRN approached Veronica Miller, PhD, Director of the Forum for Collaborative HIV Research, to write a summary of the recent XV International AIDS Conference in Bangkok, we knew that this would be a daunting task. For those interested in reading up on some of the basic science; clinical research, treatment, and care; and epidemiology and prevention data presented at the conference, we encourage readers to review the expert summaries posted on Medscape (http://www.medscape.com/viewprogram/3248) and Clinical Care Options (http://clinicaloptions.com/hiv/vp/iac2004/#download). What Dr. Miller provides us with here has not been readily available through other clinician-based publications: a personal viewpoint of the IAC and, with it, a report on some of the Forum for Collaborative HIV Research activities at the highly charged conference.

THE XV INTERNATIONAL AIDS CONFERENCE (IAC), HELD FROM JULY 11th to July 16th in Bangkok, registered 17,001 participants, 2,170 of whom were media and 750 of whom were in the student/youth category. Approximately 9,926 of us were paying delegates, and our fees contributed $8 million toward the $17 million total conference budget. With the money spent and the travel itineraries concluded, central questions remain: What did we accomplish? What will this year's IAC be remembered for?

The Priorities of Protest

AN INTERNATIONAL GATHERING OF THE SIZE THE IAC HAS GROWN TO can be a difficult-to-manage undertaking. Whereas most scientists and clinicians look for new data, new studies, and breakthroughs at major conferences, the IAC has evolved into a platform on which policy, politics, and protest appear to command more of the limelight than *bona fide* science, leaving many of the attending scientists and clinicians frustrated, confused, and disillusioned.

Protests, in one form or another, dominated this year's conference. Perhaps the massiveness of these protests should not have come as a surprise. Scientific presentations heralding yet another breakthrough for antiretroviral therapy are of little relevance to those primarily concerned with the procurement and distribution of therapy in resource-poor areas. The gap between what we already know and the global implementation of our discoveries has grown too large to be taken silently. What is it, other than the policy and politics of many governments, keeping us from doing what we have the tools to do: treat patients infected with HIV, treat their opportunistic infections, and implement prevention programs that have demonstrated success? Given the failure of the global response to provide treatment on a scale anywhere near appropriate, and given the diverse political influences on prevention and harm-reduction efforts, protest and activism was very much anticipated.

What was alarming about the Bangkok protests—both the noisy and the silent absentee kind—was that they ran the danger of closing the door to dialogue. Rather than push research forward, they may have pushed it back.

Adding a touch of irony to the various protests was the minimal financial support and limited number of delegates from the U.S. Department of Health and Human Services (DHHS). This has been perceived as a U.S. Government-enforced "absentee" counter-protest against the community protests that greeted Tommy Thompson, Secretary of Health and Human Services, at the XIV International AIDS Conference in Barcelona two years ago (Auerbach, 2004).

The problem with many of these protests in Bangkok was the unhealthy shift from protests of the constructive kind to protests of the destructive kind. Although frequently uncomfortable—and frequently very noisy—to scientists, industry, and government, activism and community participation has long pushed progress in scientific discovery, clinical research, and policy in HIV/AIDS more than in any other disease. Indeed, constructive activism opens doors to new dialogue. What was alarming about the Bangkok protests—both the noisy and the silent absentee kind—was that they ran the danger of closing the door to dialogue. Rather than push research forward, they may have pushed it back.

An example of this, which is discussed in greater detail below, was the halting of a clinical trial testing a novel approach to prevention: the efficacy of tenofovir (Viread) as preexposure prophylaxis in high-risk populations in Cambodia (Cohen, 2004). Another example was the disturbingly high number of empty poster boards, another apparent example of absentee protest, whereby scientists and/or their sponsoring institutions withheld final data presentations in an effort to say that the IAC is no longer worthy of their presence.

What is the role of clinical researchers in light of these protests? Certainly to continue cutting-edge research on the "big" questions, including working toward an effective vaccine or continuing with the development of new drugs that are less susceptible to loss of activity because of drug resistance. But while we are waiting for the big answers, researchers need to continue working on the

many, many small steps—including bioequivalence studies for generic formulations and fixed-dose combinations, efficacy of antiretroviral therapy in different populations, and behavioral and structural interventions for prevention—that will contribute to significant and measurable progress throughout the world. There is also an ongoing need to continue publishing research-based evidence to guide policy and to make clear where gaps in knowledge still exist; to integrate the research into local and regional context; to invite community participation at every possible level (not just *pro forma*); to worry less about turf and instead focus on synergizing progress through collaboration and cooperation with other programs active in the same region; and to learn from each patient as treatment is being rolled out. In short, we need to find a way to incorporate "learning as we do," as we are doing it. For those in advisory and consultancy positions, the role is to advise and consult for long-term, integrated programs. Clinical researchers need to attend conferences such as the IAC, and we need to come with an open mind to the complexities of global HIV/AIDS.

The Forum in Bangkok

THE MISSION OF THE FORUM FOR COLLABORATIVE HIV RESEARCH IS to facilitate and enhance HIV research by bringing together academia, advocacy, government, and industry in a neutral setting to identify issues that need addressing and make recommendations as to how to address those issues. The Forum sponsored three symposia during the IAC conference. One of these was: "Women and HIV: Research Directions."

The symposium, a follow-up to the 2002 "Sex and Gender in the Management of HIV Disease Care, Prevention, and Research" workshop [http://www.hivforum.org/projects/genderissues.html], was designed to focus attention on research needs specific to women and HIV. Three research themes from the frontlines of HIV care and prevention research were chosen for discussion from researchers' and community members' perspectives. They were: new approaches to prevention, addressing underlying social needs, and special needs of women in conflict and post-conflict settings.

The use of antiretrovirals in prevention of HIV infection is not a novel concept. Its efficacy in prevention of mother-to-child transmission is well established and widely accepted. As an intervention in high-risk, HIV-negative adult populations, however, the use of antiretroviral therapy as preexposure prophylaxis (aka: chemoprophylaxis) certainly is a novel approach.

Kimberly Page-Shafer, PhD, MPH, from the Center of AIDS Prevention Studies at the University of California, San Francisco, reviewed the current thinking on, and rationale for, the use of antiretrovirals by high-risk HIV-negative adults to prevent HIV infection via sexual transmission. If successful, this approach may be of significant benefit to women who are particularly and frequently vulnerable to HIV infection because of various social, economic, and biological factors. Potential benefits include prevention of HIV-1 infection, prevention of secondary cases, and availability of a personal and private prevention method that women can control (see Table 1). Dr. Page-Shafer is the principal investigator of the Cambodian HIV Prevention Study, *Kdey Sonkum Roboh Satrei* (Hope of Women), sponsored by the U.S. National Institutes of Health and Family Health International, with collaborators in Cambodia, at the University of New South Wales, and at the University of California, San Francisco.

This placebo-controlled, double-blind trial had planned to recruit 960 female HIV-negative sex workers over the age of 18 to be randomized to placebo or once-daily tenofovir. During a brief discussion period following Dr. Page-Shafer's presentation, researchers and community members alike deliberated risks and benefits. While representing hope for prevention of HIV infection in the absence of effective vaccines, this line of research raises many questions. What are the appropriate care and treatment provisions for trial participants who acquire HIV? What are the risks for development of drug resistance? Will toxicities be a problem? What is the impact on risk behavior and vulnerability? How can informed consent be assured in a research-naive population? It is this trial that would ultimately help to answer these questions.

Unfortunately, the trial, to be conducted in Cambodia, has hit several roadblocks, the last of these stopping the trial altogether. The trial was supposed to have started in June of this year. One of the earlier signs of trouble surfaced in March 2004, when a Cambodian sex workers' union, Women's Network for Unity, announced that they would not support the study unless a provision of 30 years of health

TABLE 1. Potential Benefits of Chemoprophylaxis

1. Chemoprophylaxis may prevent HIV-1 infection

- Efficacy of periexposure dosing in nonhuman primates was 50% to 100%, depending on dose and conditions.
- Efficacy of daily dosing in humans might be close to 100%.
- If there is no infection, there is no resistance.

2. Prevention of HIV-1 during chemoprophylaxis prevents secondary cases.

- People at high risk of acquiring HIV-1 also have a high risk of spreading HIV-1 to their sexual partners and infants.
- The number of secondary cases for each case depends on the numbers and types of partners (1 to 10 secondary cases expected).

3. Chemoprophylaxis, if found to be safe and effective, will provide women with a defense against HIV.

- Personal/private prevention method women control; possibly setting precedent for modifying other challenging self-protective behaviors.
- Help to overcome the limitations of condoms.
- A means of alleviating hopelessness and fatalism that may drive the HIV-1 epidemic.

Source: Kimberly Page-Shafer, PhD, MPH. Women and HIV: Research Directions, a program sponsored by the Forum for Collaborative HIV Research at the XV International AIDS Conference, Bangkok, 2004.

insurance to cover adverse reactions and side effects from taking the drug were included in the trial (*Seattle Post-Intelligencer*, March 29).

The study was then denounced at the IAC during a satellite symposium sponsored by Gilead Sciences. The protestors included the Asian Pacific Network of Sex Workers and ACT UP Paris. This time, the protest was based on demands for lifetime health care for all study participants who become infected during the study, along with accusations of "blackmail" because trial participants would receive better care and treatment than their non-participating colleagues (Cohen, 2004). More recently, on August 30, 2004, Cambodian Prime Minister Hun Sen expressed general opposition to testing HIV/AIDS drugs in Cambodians. This was followed by an instruction by the Prime Minister to the Minister of Health to stop the trial (*Wall Street Journal*, August 12).

The study team had spent considerable effort in building community support for this trial in Cambodia. The study had previously been approved by the Cambodian Ministry of Health and has the support of several other groups of sex workers. Thus, rather than provide a platform for open discussion and resolution, the protests—and subsequent government reaction—closed the door on a truly unique research approach in this region. Fortunately, similar clinical studies exploring the efficacy of tenofovir for prevention of HIV infection are ongoing in other regions, including Thailand, Western Africa, and the United States.

Prevention research has focused primarily on individual risk, behavioral change models, and technical interventions. There has been a growing recognition of the importance of structural factors, such as poverty and economic inequalities, gender inequalities, and mobility and migration and their impact on individual behavior. Interventions targeting structural factors are those that alter the context in which health is produced. These include laws and policies, cultural norms, and interventions that affect the physical environment and socioeconomic conditions. Although the importance of structural factors in health matters is recognized, few examples of studies designed to address these exist.

Julia Kim, MD, FRCP, MSc reviewed the issues associated with research of structural interventions to address underlying social/structural vulnerabilities of women to HIV infection. Barriers to structural intervention research include lack of tools to conceptualize and mount broader social and economic interventions, as well as the requirement for new partnerships across multiple sectors and disciplines, for a shift in emphasis towards concepts of community participation, and for innovative and complex experimental methods. Not least, structural interventions may challenge firmly rooted political, economic, and social interests. The disease-focused mechanisms in place make obtaining funding for this research a challenge.

Dr. Kim runs the Rural AIDS and Development Action Research (RADAR) Program, a partner in the Intervention with Microfinance for AIDS and Gender Equity (IMAGE) study. IMAGE, a multi-faceted research program, is an attempt to integrate structural interventions and HIV/AIDS prevention research. The study is a prospective, community-based randomized intervention trial among eight villages designed to develop and test interventions addressing poverty, gender, and inequalities. The interventions include microfinancing, gender and HIV training, and community mobilization. It is funded by the Ford Foundation, the Department for International Development (United Kingdom), and the Kaiser Family Foundation. Evaluation will include the impact of these interventions on a range of outcomes, including HIV incidence, at the individual, household, and community level.

Women in conflict situations frequently experience the worst that violence and gender inequality have to offer. Many Rwandan women were raped with the intent of infecting them with HIV, a very real and truly horrifying example of bioterrorism in the world. And many women, left alone after the killing of their family members, have been forced into high-risk behavior for survival.

Women in conflict situations frequently experience the worst that violence and gender inequality have to offer. Dr. Agnès Binagwaho, Executive Secretary of the National AIDS Commission Control of Rwanda, used the Rwandan experience of genocide and mass rape of Tutsi women as an example to illustrate the impact of such experience on women and society during and after the conflict period (see Table 2 on page 36). Many women were raped with the intent of infecting them with HIV, a very real and truly horrifying example of bioterrorism in the world. And many women, left alone after the killing of their family members, have been forced into high-risk behavior for survival.

With 64% of the Rwandan population living in poverty, 27% of children having lost one or both parents, and the destruction of much of the infrastructure, the national government launched a response with no prioritization for women traumatized by the war, despite the fact that the "promotion of women" in leadership positions is a primary goal of the Rwandan government. Rwandan non-government action was the real driver of the emergency response for women, organizing as communities to provide support and care. Women survivors have established trauma centers and care centers. At the moment, women survivors have access to care but not separate from the general population; plans for special programs designed for women survivors are underway. Special programs are necessary because of the double-stigma faced by these women: sexual violence and HIV/AIDS. Dr. Binagwaho finished by listing special areas of research for women, including social research to increase women's access to treatment and treatment success and behavioral research on acceptance of equality and rights for women before, during, and after war.

Kathryn Anastos MD, from the Bronx Women's Interagency Study and a member of the Women's Equity in Access to Care &

TABLE 2. Rwanda: The Social and Cultural Situation

1. Links between war and HIV

- Women raped in order to infect them with HIV.
- Women left alone because their families were killed.
- Women forced into high-risk behavior to survive; this leads to high HIV rates.

2. Links between gender and HIV

- Women are physiologically at higher risk of contracting HIV.
- Cultural issues: inequalities in income and power lead to high risk for women.
- Sexual violence becomes common in the culture, in reaction to stressful situations (psychological effects of war and trauma.

Source: Dr. Agnès Binagwaho. Women and HIV: Research Directions, a program sponsored by the Forum for Collaborative HIV Research at the XV International AIDS Conference, Bangkok, 2004.

Treatment (WE-ACTx) initiative, presented a framework for research including Rwandan women survivors of rape and genocide. The research framework is built on the maxim: "Treatment always trumps research in importance." Dr. Anastos stressed the need to seek and incorporate community and research participants' opinions and the need to develop local infrastructure that will allow sharing and transfer of control to an in-country team. Dr. Anastos has worked with the Rwandan Women's Treatment Access Initiative, a collaboration of three partners: five survivor organizations, the Rwandan government through their Treatment and Research in AIDS Care (TRAC) program within the Ministry of Health, and WE-ACTx. The goal is to provide comprehensive HIV care, including antiretrovirals and prophylaxis for opportunistic infections. The group expects to achieve this goal for 30,000 Rwandans.

Plans are also underway to establish the Rwandan Women's Cohort Study, a collaboration between the three partners listed above and the Women's Interagency HIV Study of the U.S. The collaborators will help define the research agenda, and will involve such issues as the influence of trauma on response to treatment, through biological mediators (e.g. cytokines), behavioral mediators (e.g. adherence), and biobehavioral mediators (e.g. depression and post-traumatic stress syndrome).

The short panel discussion that followed the presentations of these three research themes included Judith Auerbach, PhD (American Foundation for AIDS Research), Anne-Christine D'Adesky (WE-ACTx), Catherine Hankins, MD, MSc (The Joint United Nations Programme on HIV/AIDS), Sandra Lehrman, MD (National Insitutes of Health Division of AIDS), Glennis Mabuza (HIV South Africa), James Rooney, MD (Gilead Sciences), and Dawn Smith, MD, MS, MPH (U.S. Centers for Disease Control and Prevention). Glennis Mabuza started the discussion by reiterating the positive effect of including women participants and communities in the planning of the research studies, as well as the importance of the studies such as the IMAGE study in her community in Soweto.

The three research projects presented in this symposium—examples of three different approaches to addressing women's needs—underlined the interdisciplinary and cross-disciplinary aspects of research in the context of women's lives. More opportunities for performing research within such a framework are urgently needed.

The speakers' presentations slides are available on the Forum for Collaborative HIV Research website at www.hivforum.org. The website also contains information regarding the other two Forum-sponsored symposia at the IAC.

Conclusion

SO WHAT WILL BANGKOK BE REMEMBERED FOR? TYPICAL OF THE media, reports from the IAC focused on discontent and protests, successfully drowning out any positive messages that managed to be delivered. World leaders in HIV/AIDS also left on a somber note. To quote Anthony Fauci, Director of the National Institute of Allergy and Infectious Diseases, "We are all going to walk away from this meeting knowing we have a long way to go with regard to access, because the countries that have the greatest need still have the least access." And Dr. Jim Yon Kim, director of the Department of HIV/AIDS at the World Health Organization, left us with this comment: "All of us with the power and the responsibility to make a difference can only hang our heads in shame." Perhaps Ambassador Randall Tobias, Global AIDS Coordinator for the U.S. Department of State, summarized it best: "Preventing AIDS is not a multiple-choice test. Those who want to simplify the solution to just one method—any one method—do not understand the complexity of the problem."

What is the way forward? Acknowledging failure and the enormous complexities of the problem is a start from which new momentum and commitment need to follow. The commitment needs to come from global, regional, national, and local leaders, and include commitment to ethically sound research. We need to find a way to make true dialogue possible. This means that all voices need to be heard, and that all present need to listen. Protest and activism need to become constructive once again. *prn*

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